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EXAMINER	
BADIO, BARBARA P	

ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/676,287	HOCHBERG, RICHARD	
	Examiner	Art Unit	
	Barbara P. Badio	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 39-73 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 39-73 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Final Office Action on the Merits of a RCE

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

2. The rejection of claims 39-47 and 65-73 under 35 USC 112, first paragraph, as failing to comply with the written description requirement is withdrawn.

3. The rejection of claims 57-64 under 35 USC 112, first paragraph, as failing to comply with the written description requirement is maintained.

Applicant argues (a) an oncologist who has already treated a patient for an estrogen-sensitive cancer which resulted in remission would be able to the determine a patient at risk of a recurrence of said cancer and (b) the examples disclosed in the specification on pages 21-25 provides sufficient evidence of the general activity of the present compounds as SERMS and said activity coupled with the clinical activity of nonsteroidal SERMS provide evidence of the utility of the instant claims. Applicant's argument was considered but not persuasive for the following reasons.

Even if one agrees that an oncologist who has treated a patient for cancer would be able to determine a patient at risk of a recurrence of said cancer, the data and references cited by applicant do not provide support for "*reducing the likelihood of a recurrence of breast cancer*" in a patient.

As stated above, the claimed invention is a method of "reducing the likelihood of a recurrence of breast cancer in a patient in need thereof". Thus, the instant invention makes the assumption that the claimed compound would reduce the recurrence of breast cancer in a patient who was previously diagnosed with breast cancer but is now in remission. However, in order to make said determination, one has to be able to determine that said patient would in fact come out of remission if not treated. The present specification does not provide any guidance to enable the skilled artisan to make said determination nor is there any working example in the present specification of said reduction.

Applicant points to the examples disclosed in the present specification as evidence of the activity of the claimed compounds as SERMS and several references for support of the utility of the claimed compounds. However, upon examination of the cited references, the examiner notes that the test groups excluded patients with or suspected of breast cancer. For example, Olevsky et al. on page 791 clearly states that previous breast cancer patients were excluded.

> Exclusion criteria included the presence of known or suspected breast cancer, invasive endometrial cancer, abnormal uterine bleeding, history of stroke or venous thromboembolism, or the presence of other cancers.

. Jordan et al. on page 268 discussed the different results of three studies of the role of tamoxifen in breast cancer prevention. The studies, like those of Olevsky, do not include patients with a previous history of breast cancer. Therefore, the prior art can not provide support for "reducing the

likelihood of a recurrence of breast cancer" as claimed by the instant claims since none of the test groups included previous breast cancer patients.

For these reasons and those given in the previous Office Actions, the rejection of claims 57-64 under 35 USC 112, first paragraph, as failing to comply with the written description requirement is maintained.

4. The rejection of claims 39-47 under 35 USC 112, first paragraph, as failing to comply with the enablement requirement is withdrawn.

5. Claims 39, 42, 65, 67, 68, 70-73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating osteoporosis and control of cholesterol levels, does not reasonably provide enablement for treatment of cardiovascular disease in general. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are (1) the nature of the invention, (2) the breadth of the claims, (3) the state of the prior art, (4) the predictability or unpredictability of the art, (5) the amount of guidance or direction presented, (6) the presence or absence of working examples, (7) the relative skill in the art and (8) the quantity of experimentation necessary. When the above factors are

taken into consideration, the examiner's position is that one skilled in the art could not perform the invention commensurate in scope with the instant claim without undue experimentation.

The instant claims are drawn to a method of treating "cardiovascular" disease, i.e., a symptom of menopause. The present specification provides support by showing the agonistic/antagonistic properties and the in vivo uterotropic activity of the claimed compounds (see page 21, line 11 - page 25, line 18).

The state of the pharmaceutical art is such that screening in vitro and in vivo is utilized to determine the desired effect of pharmaceuticals. There is no absolute predictability of pharmaceuticals and, thus, one of ordinary skill in the art would not accept any therapeutic regimen on its face.

Because the pharmaceutical art is unpredictable, it requires each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F 2d. 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is the more specific enablement is needed in order to satisfy the statute.

Here, the instantly claimed invention is highly unpredictable because the skilled artisan in the art would recognize the differences in the etiology and treatment of the vast array of cardiovascular diseases. In essence, all cardiovascular diseases are not symptoms of menopause and no single agent is known to treat "cardiovascular diseases" in general. Thus, the skilled artisan would doubt the claimed compounds would be effective in treating all cardiovascular diseases.

Therefore, in the absence of a showing of correlation between all cardiovascular diseases and the effectiveness of the claimed compounds in treating said diseases, one of skill in the art would be unable to fully predict the effect of administration of the claimed compounds in the treatment of cardiovascular diseases as encompassed by the instant claims.

As stated above, the only guidance given in the present specification is a showing of the agonistic/antagonistic properties and the in vivo uterotropic activity of the claimed compounds (see page 21, line 11 - page 25, line 18), which is minimal. Thus, in order to practice the claimed invention commensurate in scope with the instant claim, the skilled artisan would have to engage in undue experimentation to determine the cardiovascular disease(s) treatable by the claimed compounds, with no assurance of success.

6. The rejection of claims 39-56 and 65-73 under 35 USC 112, second paragraph is withdrawn.

7. The rejection of claims 57-64 under 35 USC 112, second paragraph is maintained.

Contrary to applicant's statement, the term "preferably" has not been deleted from claim 57.

For this reason, the rejection of claims 57-64 under 35 USC 112, second paragraph is maintained.

Claim Rejections - 35 USC § 103

8. The rejection of claims 39-56 and 65-73 under 35 USC 103(a) over Van den Broek et al. (US 3,972,906) is maintained.

Applicant argues the reference does not teach the unique SERM activity of the claimed compounds or the use of the compounds in treating osteoporosis, cholesterolemia or elevated LDL or cardiovascular disease or to reduce the likelihood of breast cancer. Applicant's argument was considered but not persuasive for the following reasons.

Claims 39 and 65 are drawn to treating "the **symptomology of menopause**" wherein the patient populations are defined as "a patient at risk for developing estrogen-sensitive cancer" (claim 39) and "a patient with estrogen-sensitive cancer" (claim 65) utilizing the claimed compounds. The patient population of claims 39 and 65 is inclusive of any patient having any of the symptoms as recited by the instant claims. Claim 48 is a method of treating "an estrogen-sensitive cancer" in a patient in need thereof.

As stated in the previous Office Action, the steroid art teaches the use of estrogens in the treatment of menopausal syndrome as well as the treatment of breast cancer. The art also teaches menopausal syndrome is inclusive of osteoporosis, cholesterolemia, elevated LDL and atherosclerosis (a cardiovascular disease).

Van den Broek et al. teaches 11-substituted steroids such as 11β-methoxymethyl-ethinyl-estradiol, encompassed by the instant claims, for use as estrogenic agents in the treatment of estrogen-deficiency syndrome. Based on the level

of skill of the ordinary artisan in the art at the time of the present invention, the use of the compounds of Van den Broek, which are estrogenic agents, in treating estrogen-deficiency syndromes such as menopausal syndromes and in the treatment of breast cancer would have been obvious.

Applicant argues the prior art does not teach the unique SERM activity of the claimed compounds and, in fact, teaches away from the claimed invention. However, the issue is not whether the reference teaches that which was discovered by applicant, i.e., the SERM activity of the prior art compound, in order to support a legal conclusion of obviousness. The obviousness rejection is proper as long as the prior art provides a reason and/or provides a motivation to use the prior art compounds as claimed by the instant claims. In the present case, Van den Broek teaches the claimed compounds have estrogenic properties and, thus are useful in treating estrogenic deficiency syndromes. The steroid art teaches the use of estrogenic agents in the treatment of menopausal syndrome such as osteoporosis as well as breast cancer. Therefore, the prior art provides the motivation to use the compounds of Van den Broek in the claimed treatment methods.

Lastly, similar compounds would be expected to have similar properties and, thus, even though the prior art does not teach the SERM activity of the prior art compounds said activity is inherent to the prior art compounds.

For these reasons and those given in the previous Office Actions, the rejection of claims 39-56 and 65-73 under 35 USC 103(a) over Van den Broek et al. (US 3,972,906) is maintained.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Telephone Inquiry

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P. Badio whose telephone number is 571-272-0609. The examiner can normally be reached on M-F from 6:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Barbara P. Badio/
Primary Examiner, Art Unit 1612